Attorney Docket No: U0003/7017 U.S. App. No. 10/579,58

Filed: May 17, 2006

Sequence Listing and Preliminary Amendment

U.S. App. No. 10/579,581 Abdel-Wahab *et al.* Page 9

The following Listing of the Claims will replace all prior versions and all prior listings of the claims in the present application:

Listing of The Claims:

- 1-9. (Cancelled)
- 10. (Currently Amended) Peptides, or fragments thereof, as stimulators of insulin secretion and pancreatic beta cell function, each peptide having at least 50% sequence identity based on the ClustalW alignment method with sequences selected from the group comprising AVITGACERDVQCGGGTCCAVSLI (SEQ ID NO:18) and the respective amino acid sequences of SEQ ID Nos. 1 to 17, each peptide being selected from the group comprising:

a peptide having at least 50% sequence identity based on the ClustalW alignment method with the amino acid sequence of dermaseptin and the partial structure A-WKD-LKN-GKAAGKAVLN-VTDMVN- (SEQ ID NO:19)

a peptide having at least 50% sequence identity based on the ClustalW alignment method with a peptide having a structure selected from the group comprising the partial structure KG----LL--ASCKLS—C (SEQ ID NO:20), the structure SEQ ID No. 6 GKPFYPPPIYPEDM (peptide 24, *Bombina variegata*), the partial structure FLP--AG-AA---PKIFC-I—KC (SEQ ID NO:21) and SEQ ID No. 10 ALSILRGLEKLAKMGIALTNCKATKKC (peptide 3.8, *Rana palustris*);

a peptide having at least 50% sequence identity based on the ClustalW alignment method with the amino acid sequence of esculentin and the partial structure GIFSK----KK-KNLLISGLKNVGKEVGMDVVRTGIDIAGCKIKGEC (SEQ ID NO:22);

a peptide having at least 50% sequence identity based on the ClustalW alignment method with the amino acid sequence of bombesin and the peptide having the partial structure ---G-QWA-GH-M (SEQ ID NO:23); and

a peptide having at least 50% sequence identity based on the ClustalW alignment method with the amino acid sequence of a peptide selected from the group comprising AVITGACERDVQCGGGTCCAVSLI (SEQ ID NO:18), SEQ ID No. 1

U.S. App. No. 10/579,581

Attorney Docket No: U0003/7017

Filed: May 17, 2006

Sequence Listing and Preliminary Amendment

Abdel-Wahab *et al.*Page 10

RRKPLFPFIPRPK (peptide 1.10, *Agalychnis calcarifer*), SEQ ID No.7 IYNAICPCKHCNKCKPGLLAN (peptide 25, *Bombina variegata*), SEQ ID No. 2 a peptide having the N-terminus sequence MLADVFEKIMGD... (N-terminus of peptide 1.7, *Agalychnis litodryas*) and SEQ ID No. 8 a peptide having the N-terminus sequence XXPLAPFFQAVFK... (N-terminus of peptide 1.8, *Phyllomedusa trinitatis*).

- 11. (Currently Amended) A peptide according to Claim 10, in which each peptide has at least 80% sequence identity based on the ClustalW alignment method with sequences selected from the group comprising AVITGACERDVQCGGGTCCAVSLI (SEQ ID NO:18) and the respective amino acid sequences of SEQ ID Nos. 1 to 17.
- 12. (Currently Amended) A peptide according to Claim 10, in which each peptide has at least 90% sequence identity based on the ClustalW alignment method with sequences selected from the group comprising AVITGACERDVQCGGGTCCAVSLI (SEQ ID NO:18) and the respective amino acid sequences of SEQ ID Nos. 1 to 17.
- 13. (Currently Amended) A peptide according to Claim 10, in which each peptide has more than 95% sequence identity based on the ClustalW alignment method with sequences selected from the group comprising AVITGACERDVQCGGGTCCAVSLI (SEQ ID NO:18) and the respective amino acid sequences of SEQ ID Nos. 1 to 17.
- 14. (Previously presented) A peptide according to Claim 10, in which the peptide is selected from SEQ ID No. 3 AVWKDFLKNIGKAAGKAVLNSVTDMVNE (peptide 2.9, *Agalychnis litodryas*) and SEQ ID No. 9

 ALWKDILKNVGKAAGKAVLNTVTDMVNQ (peptide 2.10, *Phyllomedusa trinitatis*).
- 15. (Currently Amended) A peptide according to Claim 10, in which the partial structure is GIL—LK-FA—AGKG----LL—ASCKLSGQC (SEQ ID NO:24).

Attorney Docket No: U0003/7017 U.S. App. No. 10/579,581

Filed: May 17, 2006

Sequence Listing and Preliminary Amendment

Abdel-Wahab *et al*. Page 11

16. (Previously presented) A peptide according to Claim 15, in which the peptide is selected from SEQ ID No. 12 KGAAKGLLEVASCKLSKSC (peptide 4.22, *Rana saharica*), SEQ ID No. 15 GILSTIKDFAIKAGKGAAKGLLEMASCKLSGQC (peptide 5.6, *Rana saharica*) and SEQ ID No. 16 GILLDKLKNFAKTAGKGVLQSLLNTASCKLSGQC (peptide 6.5, *Rana saharica*).

- 17. (Previously presented) A peptide according to Claim 10, in which the peptide is selected from the group comprising SEQ ID No. 11 FLPIIAGVAAKVFPKIFCAISKKC (peptide 4.1, *Rana pipiens*) and SEQ ID No. 17 FLPLLAGLAANFLPKIFCKITRKC (peptide 8.3, *Rana saharica*).
- 18. (Currently Amended) A peptide according to Claim 10, in which the peptide has the partial structure GIFSK---KK-KNLLISGLKNVGKEVGMDVVRTGIDIAGCKIKGEC (SEQ ID NO:22), the peptide being selected from SEQ ID No. 13 GIFSKFGRKKIKNLLISGLKNVGKEVGMDVVRTGIDIAGCKIKGEC (peptide 5.1 Rana saharica) and SEQ ID No. 14 GIFSKLAGKKLKNLLISGLKNVGKEVGMDVVRTGIDIAGCKIKGEC (peptide 5.4 Rana saharica).
- 19. (Currently Amended) A peptide according to Claim 10, in which the partial structure is ---G-QWA-GH-M (SEQ ID NO:23), the peptide being selected from the group comprising SEQ ID No. 4 Pyr-QRLGHQWAVGHLM-amidated (peptide 21, *Bombina variegata*) and SEQ ID No. 5 Pyr-DSFGNQWARGHFM-amidated (peptide 22, *Bombina variegata*).
- 20. (Previously presented) A peptide as claimed in Claim 10 with at least one amino acid modification by insertion of fatty acid at the alpha amino group of native amino acid or an epsilon amino group of a substituted lysine residue.

Attorney Docket No: U0003/7017 U.S. App. No. 10/579,581

Filed: May 17, 2006

Sequence Listing and Preliminary Amendment

Abdel-Wahab et al. Page 12

21. (Previously presented) A peptide as claimed in Claim 10, having at least one amino acid substitution and/or modification including N-glycated, N-alkylated, N-acetylated, Nacylated, N-isopropyl, and / or N-pyroglutamyl amino acids.

- 22. (Previously presented) A pharmaceutical composition including at least one peptide according to Claim 10 in admixture with a pharmaceutically acceptable excipient.
- 23. (Previously presented) A pharmaceutical composition including at least one peptide according to Claim 14 in admixture with a pharmaceutically acceptable excipient.
- 24. (Previously presented) A pharmaceutical composition including at least one peptide according to Claim 16 in admixture with a pharmaceutically acceptable excipient.
- 25. (Previously presented) A pharmaceutical composition including at least one peptide according to Claim 17 in admixture with a pharmaceutically acceptable excipient.
- 26. (Previously presented) A pharmaceutical composition including at least one peptide according to Claim 18 in admixture with a pharmaceutically acceptable excipient.
- 27. (Previously presented) A pharmaceutical composition including at least one peptide according to Claim 19 in admixture with a pharmaceutically acceptable excipient.
- 28. (Previously presented) A pharmaceutical composition as claimed in Claim 22 which further comprises at least one further pharmaceutically active agent, the, or each, further pharmaceutically active agent being selected from one or more sulphonylureas, meglitinides, metformin, and/or thiazolidinediones, or a mixture thereof.
- 29. (Previously presented) A pharmaceutical composition as claimed in Claim 22, the pharmaceutical composition being for delivery through transdermal, nasal inhalation, oral or injected routes.

Attorney Docket No: U0003/7017 U.S. App. No. 10/579,581

Filed: May 17, 2006

Sequence Listing and Preliminary Amendment

Abdel-Wahab *et al.* Page 13

30. (Previously presented) A method for stimulating insulin secretion by activation of physiological stimulus-secretion coupling pathways, rather than by antimicrobial action involving cell lysis, the method comprising administering to an individual an effective amount of the peptide selected from the group comprising brevinins, dermaseptins, esculentins and peptides, or fragments thereof, as claimed in Claim 10.

- 31. (Previously presented) A method to stimulate insulin secretion and / or moderate blood glucose excursions, the method comprising administering to an individual an effective amount of a peptide selected from the group comprising brevinins, dermaseptins, esculentins and peptides, or fragments thereof, as claimed in Claim 10.
- 32. (Previously presented) A method to stimulate insulin secretion and / or moderate blood glucose excursions, the method comprising administering to an individual an effective amount of peptides, or fragments thereof, as claimed in Claim 10.
- 33. (Previously presented) A method to stimulate insulin secretion and / or moderate blood glucose excursions, the method comprising administering to an individual an effective amount of peptides, or fragments thereof, as claimed in Claim 14.
- 34. (Previously presented) A method to stimulate insulin secretion and / or moderate blood glucose excursions, the method comprising administering to an individual an effective amount of peptides, or fragments thereof, as claimed in Claim 16.
- 35. (Previously presented) A method to stimulate insulin secretion and / or moderate blood glucose excursions, the method comprising administering to an individual an effective amount of peptides, or fragments thereof, as claimed in Claim 17.

Attorney Docket No: U0003/7017

Filed: May 17, 2006

Sequence Listing and Preliminary Amendment

U.S. App. No. 10/579,581

Abdel-Wahab et al.

Page 14

36. (Previously presented) A method to stimulate insulin secretion and / or moderate blood glucose excursions, the method comprising administering to an individual an effective amount of peptides, or fragments thereof, as claimed in Claim 18.

- 37. (Previously presented) A method to stimulate insulin secretion and / or moderate blood glucose excursions, the method comprising administering to an individual an effective amount of peptides, or fragments thereof, as claimed in Claim 19.
- 38. (Previously presented) A method for the treatment of type 1 or type 2 diabetes mellitus, the method comprising administering to an individual an effective amount of a peptide selected from the group comprising brevinins, dermaseptins, esculentins and peptides, or fragments thereof, as claimed in Claim 10.